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Rubella antibody loss rates in Korean children

M. KI[1], M. H. KIM[1], B. Y. CHOI[2]*, Y. J. SHIN[2] AND T. PARK[3]

[1] *Department of Preventive Medicine, Eulji University School of Medicine, Daejon, Korea*
[2] *Department of Preventive Medicine, Hanyang University College of Medicine, Seoul, Korea*
[3] *Department of Statistics, Seoul National University, Seoul, Korea*

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SUMMARY

We followed students in eight elementary schools for rubella antibody from 1993 to 1996 (602 pairs) and 1996–9 (588 pairs) in Gyeonggi Province, Korea. We tested rubella IgG and administered rubella vaccine to the children with the titres <10 IU/ml. The loss rates of rubella IgG during the follow-up periods were 14·3 and 15·8%, respectively. Among vaccinated groups, the loss rate was 18·8%, which was significantly higher than 13·8% of the mixture of natural and vaccine-induced immunity groups. The group that had the lower preceding antibody titre had a higher loss rate of 24·8% compared to 7·2% for the group whose titre was 40 IU/ml or above. In a multivariate analysis, age and gender were not related to antibody loss rate. Under this higher rubella antibody loss rate, in order to prevent congenital rubella syndrome, the immunization for women at childbearing age appears necessary until rubella can be eliminated or controlled.

INTRODUCTION

The primary objective of a rubella immunization programme is to prevent the congenital rubella syndrome (CRS) [1]. For this purpose, vaccine-induced rubella-specific immunity should persist to and throughout childbearing age in women. Several studies have shown that vaccines induce long-lasting antibody responses of up to 23 years [2]. Many studies argue that the antibody loss rates differ with vaccine strains and study areas where wild rubella viruses circulate [3, 4]. However, the difference was very small. The annual antibody loss rates varied from 0 to 1% and most studies report about 0·5% [5–9]. However, even in the closed population, the annual antibody loss rate was 0·67% [2]. One of the reasons for similar antibody loss rates in those studies was that the vaccination schedules were similar to the early 1970s. Long-term follow-up studies provide good information, but the subjects were vaccinated 10–20 years ago, so there is no useful information about the durability for recent vaccine-induced immunity. A recent report using a study area with high vaccination coverage where immunity was induced by two doses of measles, mumps and rubella (MMR) vaccine showed the proportion with rubella virus-specific IgG antibody titres below 15 IU/ml were 31%. This was the titre 15 years after the first vaccination and 11 years after the second vaccination [10]. This demonstrates that rubella re-infection could occur in those with reduced immunity [11–13], and if occurring during pregnancy, may cause congenital rubella syndrome [14–16]. Therefore, the rubella sero-epidemiological study should be concerned with the lower immunity group, who could be infected, and the recent vaccine-induced immunity group in the 1990s.

* Author for correspondence: Department of Preventive Medicine, Hanyang University College of Medicine, 17 Haengdang-dong, Sungdong-gu, Seoul, 133-791, South Korea.

In Korea, rubella had not been a notifiable disease until 2000, and CRS was not a notifiable disease until now. There is insufficient data on the incidence of rubella and CRS. Like measles and mumps, rubella has also occurred as periodic epidemics every 4–5 years. In outbreaks during March–April 1996, 4581 cases of rubella were reported to the national centres by a temporary surveillance system [17]. This outbreak also occurred among the vaccinated student population. At that time, the incidence rate was at the highest, 67·5 per 100 000 in the group aged 15–19 years, and next highest at 44·7 per 100 000 in the 10–14 years old age group. The cause was presumed to be the low vaccine coverage rate and waning of the immunity induced by the vaccine. From the mid-1980s, MMR vaccines were generally used in Korea. Additionally, since 1997, a second dose of MMR vaccine has been recommended to children aged 4–6 years. We could not clearly pinpoint the cause of the outbreak and cannot anticipate how often outbreaks will occur among the vaccinated population.

In this study, we report the antibody loss rates, including the immunity by vaccination in 1993 or 1996, and the related factors in Korean children. We observed 602 and 588 children in eight elementary schools during 1993–6 and 1996–9, respectively.

METHODS

Study subjects and samples

Study areas were in the Gyeonggi Province which borders on Seoul, the capital of Korea. We selected eight elementary schools according to location, four of which are located in rural areas, and the rest in urban; and each of them are located to the east, west, south and north of Seoul. The eight elementary schools were 10–50 km from the border of Seoul. We surveyed these schools repeatedly in 1993, 1996 and 1999. Questionnaires were completed and blood samples were taken for serology tests. In 1996 and 1999, we followed the students who participated in the survey 3 years previously. After testing for rubella virus-specific IgG antibody, we notified the results to the teachers and the parents of all study subjects. For students whose IgG antibody titre was negative, we administered the rubella vaccine free of charge and then determined rubella virus-specific IgG 2–3 months later.

A detailed flow chart of the first survey and the follow-up survey is shown in Figure 1(*a*, *b*).

Questionnaires

We surveyed the demographic characteristics and the vaccination history by using questionnaires. In the questionnaire, age, gender, and identification number of the students, monthly income, education levels and occupations of parents, status of mandatory vaccinations by vaccination records, and the histories of vaccine-preventable disease infection were included. Since the study subjects were elementary school students, their parents completed the questionnaires.

Vaccination

Two kinds of rubella monovalent vaccines were administered to the rubella virus antibody-negative children. The vaccine strains were Takahashi and Matsuura, which were manufactured by the Kitasato Institute of Japan and Osaka University of Japan, respectively. The vaccines of Takahashi strain were administered in schools of the west and south in 1993, and in schools of the east and north in 1996. Those of Matsuura strain were administered in the remaining schools.

Serological tests

With the informed consent of the parents, blood samples were obtained through venepuncture. The sera were separated and stored at -70 °C until tested. Rubella virus-specific IgG antibodies were measured quantitatively by use of commercial immunoassay kits (IMx® Abbott, USA for 1993 and 1999, and Enzygnost® Behring, Germany for 1996). Although they were not evaluated in a Korean population, the sensitivity, specificity and accuracy of Abbott's IMx were 99·9, 98·9 and 99·8%, respectively [18]. For the Behring's Enzygnost, the sensitivity and specificity were 100 and 98·5%, respectively [19]. According to our tests with the two methods for quality control, there were no significant differences in titres of IgG between IMx and Enzygnost.

Specific IgG positivity indicates having immunity against rubella. However, there are various opinions on the cut-off level which equates with immune status. In this study, we determined the titre 10 IU/ml or above as positive, according to the Rubella Subcommittee of the National Committee for Clinical Laboratory Standards (NCCLS) [20].

Statistical analysis

We analysed the data using the Statistical Package SPSS 10.0 for Windows. We used a 5% significance

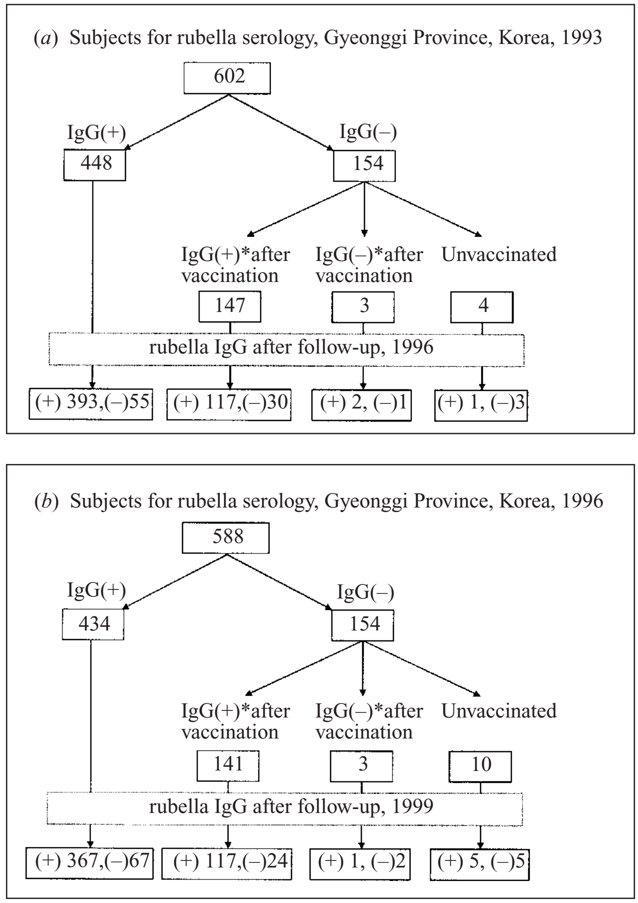

Fig. 1. Flow chart of the study, Korea (*a*) 1993–6, (*b*) 1996–9. * Rubella test was carried out (*a*) 3 months, (*b*) 2 months after vaccination.

level. Rubella virus antibody negative samples were excluded in computing geometric mean titre (GMT)s. We used the χ^2 test for comparing the antibody loss rates. We fitted the logistic regression model for estimating the adjusted odds ratios.

RESULTS

General characteristics of study subjects

Questionnaires and serological surveys were carried out in eight elementary schools in 1993, 1996 and 1999. In 1996, we followed 602 students who were in grades 1–3 in 1993. In 1999, we followed 588 students who were in grades 1–3 in 1996. The follow-up rates were 59·5% for 1996 and 59·6% for 1999. Non-respondents who did not participate in the follow-up surveys were students who transferred to other schools. The school year distributions by survey year were not different (Table 1).

The age range was 6–10 years, and the distribution of age was not uniform. Gender distributions by survey year were not different. The study subjects were 563 students (47·3%) for urban areas and 627 students (52·7%) for rural areas. Socioeconomic status was measured by parental education level, which was determined by the higher level between the mother and the father. Parental education levels became higher according to the consecutive survey years; the percentage at middle school and below was 22·4% in 1993 and 10·7% in 1996 (Table 2).

Among the rubella virus antibody negative students, 9 of 20 seroconverted during the follow-up period, but none of the seroconverted students were reported with clinical rubella symptoms in the questionnaire or the surveillance system. The school-based surveillance system for infectious disease was developed and managed by the authors since 1997. About 70 representative schools throughout Korea including these eight elementary schools participated in this surveillance system, and the data were collected every week by teachers of schools using fax or the Internet. Therefore the subclinical rubella infection must have occurred during the follow-up period (Fig. 1 *a*, *b*).

Table 1. *Number of subjects and follow-up rates by school years*

School years at the first survey	First survey in 1993 (*n*)	Follow-up survey in 1996 (*n*)	Follow-up rate (%)	First survey in 1996 (*n*)	Follow-up survey in 1999 (*n*)	Follow-up rate (%)
First	343	204	59·5	331	191	57·7
Second	331	187	56·5	330	192	58·2
Third	337	211	62·6	325	205	63·1
Total	1011	602	59·5	986	588	59·6

Table 2. *Demographic characteristics of subjects by surveys*

	1993–6 pairs tested		1996–9 pairs tested		Total pairs tested	
Characteristics	*n*	%	*n*	%	*n*	%
Age at the first survey						
6	80	13·3	36	6·1	116	9·7
7	192	31·9	183	31·1	371	31·5
8	209	34·7	201	34·2	410	34·5
9	112	18·6	163	27·7	276	23·1
10	9	1·5	5	0·9	14	1·2
*P**		0·000		0·000		0·000
Gender						
Male	310	51·5	306	52·0	616	51·8
Female	292	48·5	282	48·0	574	48·2
*P**		0·463		0·322		0·223
Area						
Urban	278	46·2	285	48·5	563	47·3
Rural	324	53·8	303	51·5	627	52·7
*P**		0·061		0·458		0·064
Parental education level						
⩽Middle school	135	22·4	63	10·7	198	16·6
High school	324	53·8	294	50·0	618	51·9
⩾College	87	14·5	112	19·0	199	16·7
*P**		0·000		0·000		0·000
Missing	56	9·3	119	20·2	175	14·7
Total	602	100·0	588	100·0	1190	100·0

* *P* value obtained by χ^2 test.

Rubella IgG antibody loss rates

The rubella IgG antibody loss rate during the follow-up periods was 15·0% (176/1170) (95% confidence interval 13·0–17·2%). The differences between the follow-up periods were not significant ($P=0{\cdot}488$). The antibody loss rates by age and parental education level were not significantly different in both the 1993–6 and the 1996–9 follow-up. Antibody loss rates in urban areas (16·1%) were higher than those of rural areas (12·7%) in the 1993–6 follow-up, but significantly lower in the 1996–9 follow-up (11·2%, 20·2%). However, it was caused by the different loss rates by the schools and the survey years. In urban or rural areas, the antibody loss rates were significantly different by the location of the schools. Particularly, the east rural schools had the lowest antibody loss rate (1·7%) in the 1993–6 follow-up, and the east urban schools had the lowest antibody loss rate (1·2%) in the 1996–9 follow-up. In the 1993–6 follow-up, the west urban and rural schools had the highest antibody loss rates, 27·8 and 27·6%, respectively. The loss rates of males were higher than those of females in the 1993–6 and 1996–9 follow-up, and the overall differences were significant ($P=0{\cdot}039$). The antibody titres in the first survey were significantly related to the antibody

Table 3. *Rubella IgG antibody loss rates during 3 years by related factors*

Characteristics	1993–6 Pairs tested	1993–6 % antibody loss	1996–9 Pairs tested	1996–9 % antibody loss	Total Pairs tested	Total % antibody loss
Age at first survey						
6–7	268	14·2	217	12·0	485	13·2
8	208	15·9	194	18·0	402	16·9
9–10	119	11·8	164	18·3	283	15·5
*P**		0·593		0·144		0·293
Gender						
Male	306	16·3	295	18·0	601	17·1
Female	289	12·1	280	13·6	569	12·8
*P**		0·141		0·149		0·039
Location of school						
East Urban	68	20·6	81	1·2	149	10·1
Rural	58	1·7	105	19·0	164	12·8
West Urban	54	27·8	65	10·8	119	18·5
Rural	76	27·6	59	18·8	135	23·7
South Urban	70	10·0	62	19·4	132	14·4
Rural	97	9·3	72	19·4	169	13·6
North Urban	81	9·9	70	15·7	151	12·6
Rural	90	11·1	61	24·6	151	16·6
*P**		0·000		0·005		0·054
Immunity type						
Vaccine-induced	147	20·4	141	17·0	288	18·8
Mixture of natural and vaccine-induced	448	12·3	434	15·4	882	13·8
*P**		0·014		0·654		0·043
Preceding IgG titre (IU/ml)						
10–39·9	230	24·3	291	25·1	521	24·8
⩾40·0	365	7·9	284	6·3	649	7·2
*P**		0·000		0·000		0·000
Total	595	14·3	575	15·8	1170	15·0

* *P* value obtained by χ^2 test.

loss rates ($P = <0{\cdot}001$). Among the low titre group (10–39·9 IU/ml), the antibody loss rate during the follow-up periods was 24·8 %, which was higher than the 7·2 % loss rate in the high titre group (⩾40 IU/ml). We classified the immunity type of students into two groups; the vaccine-induced immunity group was composed of students who seroconverted by vaccination after the rubella antibody test in the first survey, while the mixture immunity group was composed of vaccine- or natural infection-induced immunity, which had a rubella antibody titre > 10 IU/ml in the first test of the survey. The vaccine-induced immunity group had a significantly higher loss rate than that of the mixture immunity group in the 1993–6 follow-up (Table 3).

Among the related factors, age at the first survey and the location of the schools showed interaction with the survey years. However, the interaction between age at the first survey and the survey year was not significant. So, the model for multiple logistic regression analysis was:

$$\begin{aligned}\text{Logit}(\text{Ab loss}_i) &= \beta_0 + \beta_1 \text{ survey year} + \beta_2 \text{ age} \\ &+ \beta_3 \text{ gender} + \beta_4 \text{ preceding Ab titre group} \\ &+ \beta_5 \text{ immunity type} + \beta_{6-12} \text{ school (1–7)} \\ &+ \beta_{13-19} \text{ survey year} \times \text{school} \\ &+ e_i \ (i = 1, \ \ldots, 1170).\end{aligned}$$

The age at the first survey was also not related to the antibody loss rates in the multivariate analysis. Contrary to univariate analyses, gender was not significant in the multivariate analyses. The preceding antibody titre was significant and the odds ratio increased from 4·2 in the univariate analyses to 9·4 in

Table 4. *Crude and adjusted odds ratios* (*OR*) *on rubella virus antibody loss rates**

Variable	Crude OR	Adjusted OR	95% CI
Age	1·1	0·96	0·80–1·2
Gender (M/F)	1·4†	1·2	0·85–1·7
Preceding antibody titre (10–39·9/40 IU/ml)	4·2†	9·4	6·2–14·7
Immunity type (vaccine-induced /mixture of natural and vaccine-induced)	1·4†	3·7	2·4–5·7

* Model: Logit(antibody loss_i) = $\beta_0+\beta_1$ survey year + β_2 age + β_3 gender + β_4 antibody titre group + β_5 immunity group + β_{6-12} school $(1\sim7)$ + β_{13-19} survey year × school + e_i $(i=1, \ldots, 1170)$.
† $P<0.05$.

multivariate analyses. The immunity type was also strongly related to the antibody loss rate, and the odds ratio increased from 1·4 to 3·7 in the multivariate analyses (Table 4).

Rubella virus-specific IgG antibody titre

During the follow-up periods, the subjects with decreased titres were 82·4 and 79·3%, in the 1993–6 and the 1996–9 follow-up, respectively. The subjects with increased titres of 1- to 3-fold, which had a booster effect from the subclinical rubella infection, were 14·3 and 19·4%, respectively. The subjects with fourfold increased titres, which indicates that they had rubella reinfection, were 3·3% in the 1993–6 follow-up and 1·4% in the 1996–9 follow-up. The GMTs of the subjects in the first surveys before vaccination were 25·2 IU/ml in 1993 and 20·8 IU/ml in 1996. After rubella vaccinations to rubella virus antibody negative students, the GMTs increased to 48·1 and 39·0 IU/ml in 1993 and 1996, respectively. However, during the follow-up periods, the GMTs decreased to 27·4 and 22·5 IU/ml, respectively. The GMT differences among the decreased titres group were 21·2 and 17·2 IU/ml, which indicate that the annual decrease in titres was 7·1 IU/ml during 1993–6 and 5·7 IU/ml during 1996–9 (Table 5).

Seroconversion rates by strain were not different between Takahashi and Matsuura, 99·3% (438/441) and 98·5% (449/456), respectively. GMTs after vaccination were significantly different between Takahashi and Matsuura; in 1993, 108·7 and 59·1 IU/ml, respectively, and in 1996, 97·2 and 34·7 IU/ml, respectively (Ki et al.).

DISCUSSION

Rubella virus-specific IgG antibodies induced by rubella vaccine (Takahashi and Matsuura strains) have been maintained at a protective level for 3 years with 81% of the vaccinees. Mixture immunity of the natural infection and the vaccine-induced have been maintained at 86%, which was significantly higher than that of the vaccine-induced immunity group.

In this study, the sera were tested immediately after the survey. However, we could not use the same ELISA tests in both time periods, which could have been a source of measurement bias. Thus, a statistical test was performed for comparing two ELISA methods; IMx and Enzygnost. The subjects for the test were 12 pregnant women who were on a regular check-up visit. We collected the data from one hospital. The sera were diluted 1 in 2, 1 in 4 and 1 in 8 and tested by the two ELISA methods. Using the mixed model for repeated measures data, we performed a test to see whether the results of the two ELISA methods differed [21]. There was no significant difference between the results provided by the two ELISA tests ($P=0.5915$).

In this study, the age distribution of subjects was not uniform because the survey used children from grades 1–3, and the students who entered school a little earlier or later could be included in those grades. Therefore, we analysed the data by groups aged 6–7, 8 and 9–10 years of age. The area distribution was not significantly different because we selected the subject schools by area. As urbanization increased in Korea, two rural areas changed into cities in 1999. However, we analysed the data by first area classification because the two schools remained in a rural community. The percentage of parents who graduated from high school and beyond were 68·3% in 1993, and 69·0% in 1996. However, the percentage of those who graduated from middle school and below decreased from 22·4% in 1993 to 10·7% in 1996. As time passes, the education level of the population increases. The percentage of subjects who were included in the missing group would also differ in education level.

In this study, the antibody titres induced by the Takahashi and Matsuura rubella vaccine strains also dropped after 3 years. The difference between Takahashi and Matsuura vaccines was not calculated. Most studies that used RA27/3 strain reported a long-lasting antibody titre [8, 9, 22]. However, one paper reported that antibody levels dropped significantly in 6 of 15 cases, 24–27 months after revaccination [23]. Another

Table 5. *Rubella IgG antibody titres by surveys*

Characteristics	1993–6		1996–9		Total	
	n	%	*n*	%	*n*	%
Titre decreased	496	82·4	466	79·3	962	80·8
1- to 3-fold increased	86	14·3	114	19·4	200	16·8
4-fold increased	20	3·3	8	1·4	28	2·4
	n	IU/ml	*n*	IU/ml	*n*	IU/ml
GMT* at first survey before vaccination	562	25·2	588	20·8	1149	22·9
GMT at first survey after vaccination	602	48·1	588	39·0	1189	43·3
GMT at follow-up survey	602	27·4	588	22·5	1189	24·9
GMT differences among decreased	496	21·2	466	17·2	962	19·2

* GMT, geometric mean titre.

Japanese rubella vaccine, the Matsuba strain, was shown to induce immunity for 23 years in a closed population, except in 4 cases (15·4%), which had reverted to rubella antibody negative [2]. In this study, lower titre was strongly related to the antibody loss rate. So the titre after immunization can be a proxy variable for estimating the antibody retention duration.

One report based on a population study in Korea has shown the rubella infection rate in pregnant women was 0·9% (95% CI 0·4–1·8%) and the overall positive rate of rubella IgG antibody detected by MEIA was 94·5% (826/874). Moreover, the positive rate significantly increased as age increased, and reached 100% in pregnant women who were over 35 years old, indicating that a large number of women are infected during their childbearing years [24]. The subjects of that report were part of the unvaccinated population so the immunity was from natural infection. Therefore, the percent of those susceptible and the low titres increases as the percent of vaccination coverage increases and natural infection decreases.

In Korea, universal immunization of children of both sexes to suppress the circulation of the virus started in the 1980s. However, the selective immunization programme for schoolgirls and non-immune women at childbearing age was not in place. In 1994, the selective immunization programme for high-school girls started. As a result, the rubella outbreaks continued and in 1996, a nationwide outbreak occurred. The vaccination coverage rate for MMR among these subjects was 85·5% in 1996 and 83·0% in 1999, respectively. Although, a two-dose programme with a combined vaccine against measles, mumps and rubella has been recommended since 1997, the vaccination rate for the second dose was below 30% [25]. From our results, the loss rate of vaccine-induced immunity was high. Therefore, the immunization rate was not high enough to be able to protect against the rubella epidemic.

Rubella re-infection has been reported in both naturally and vaccine-induced immunity [26, 27]. Rare cases of re-infection with rubella have been reported in mothers who had been confirmed to have rubella antibodies acquired by natural infection or vaccination [14, 15, 28]. Such problems may be resolved by the elimination of rubella. So, until that time, in order to prevent congenital rubella syndrome, the immunization for women at childbearing age appears necessary.

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REFERENCES

1. Center for Disease Control and Prevention. Measles, mumps, and rubella – vaccine use and strategies for elimination of measles, rubella and congenital rubella syndrome and control of mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1998; **47**: 1–57.
2. Asahi T, Ueda K, Hidaka Y, Miyazaki C, Tanaka Y, Nishima S. Twenty-three year follow-up study of rubella antibodies after immunization in a closed population,

and serological response to revaccination. Vaccine 1997; **16**: 1791–5.
3. Schiff GM, Rauh JL, Young B, Trimble S, Rotte T, Schiff BE. Rubella-vaccinated students, follow-up in a public school system. JAMA 1978; **240**: 2635–7.
4. Farquhar JD. Follow-up on rubella vaccinations and experience with subclinical reinfection. J Pediatr 1972; **81**: 460–5.
5. Chu SY, Bernier RH, Stewart JA, et al. Rubella antibody persistence after immunization: sixteen-year follow-up in the Hawaiian Islands. JAMA 1988; **259**: 3133–6.
6. Boulianne N, Serres GD, Ratnam S, Ward BJ, Joly JR, Duval B. Measles, mumps, and rubella antibodies in children 5–6 years after immunization: effect of vaccine type and age at vaccination. Vaccine 1995; **13**: 1611–6.
7. Hermann KL, Halstead SB, Wiebenga NH. Rubella antibody persistence after immunization. JAMA 1982; **247**: 193–6.
8. Balfour HH Jr, Groth KE, Edelman CK. RA27/3 Rubella vaccine, a four year follow-up. Am J Dis Child 1980; **134**: 350–3.
9. Christenson B, Bottiger M. Long-term follow-up study of rubella antibodies in naturally immune and vaccinated young adults. Vaccine 1994; **12**: 41–5.
10. Davidkin I, Peltola H, Leinikki P, Valle M. Duration of rubella immunity induced by two-dose measles, mumps and rubella (MMR) vaccination. A 15-year follow-up in Finland. Vaccine 2000; **18**: 3106–12.
11. O'Shea S, Best JM, Banatvala JE. Viremia, virus excretion, and antibody response after challenge in volunteers with low levels of antibody to rubella virus. J Infect Dis 1983; **148**: 639–47.
12. Cusi MG, Rossolini GM, Valensin PE, Cellesi C, Zanchi A. Serological evidence of reinfection among vaccinees during rubella outbreak. Lancet 1990; **336**: 1071–3.
13. Cusi MG, Valensin PE, Cellesi C. Possibility of reinfection after immunization with RA 27/3 live attenuated rubella virus. Arch Virol 1993; **129**: 337–40.
14. Behrman RE, Kliegman RM, Arvin AM. Nelson textbook of pediatrics, 15th ed. Philadelphia: WB Saunders Co., 1995; 527–8, 871–3.
15. Paludetto R, van dn Heuvel J, Stagni A, Grappone L, Mansi G. Rubella embryopathy after maternal reinfection. Biol Neonate 1994; **65**: 340–1.
16. Hornsten L, Levy U, Fogel A. Clinical rubella with transmission to the fetus in a pregnant woman considered to be immune. N Engl J Med 1988; **391**: 1415–6.
17. National Institute of Health-Korea. Communicable Diseases Monthly Report 1996; **7**: 41.
18. Schaefer LE, Dyke JW, Meglio FD, Murray PR, Crafts W, Niles AC. Evaluation of microparticle enzyme immunoassays for immunoglobulins G and M to rubella virus and *Toxoplasma gondii* on the Abbott IMx automated analyzer. J Clin Microbiol 1989; **27**: 2410–3.
19. Behring. Enzygnost® Anti-Rubella-Virus/IgG Package Insert, 1998.
20. Skendzel LP. Rubella immunity. Defining the level of protective antibody. AJCP 1996; **106**: 170–3.
21. Jennrich RI, Schluchter MD. Unbalanced repeated-measures models with structured covariance matrices. Biometrics 1986; **42**: 805–20.
22. Horstmann DM, Schluederberg A, Emmons JE, Evans BK, Randolph MF, Andiman A. Persistence of vaccine-induced immune response to rubella comparison with natural infection. Rev Infect Dis 1985; **7**: s80–5.
23. Serdula MK, Halstead SB, Wiebenga NH, Herrmann KL. Serological response to rubella revaccination. JAMA 1984; **251**: 1974–7.
24. Ki M, Choi BY, Shin YJ, Park HB, Youn BJ, Han JS. A seroepidemiologic study on rubella antibody in pregnant women in Kyonggi-do. Korean Prevent Med 1997; **30**: 279–92.
25. Ki M, Kim MH, Shin YJ, Choi BY. MMR immunization rate and related factors. J Korean Pediatr Soci 2001; **44**: 375–88.
26. Weibel RE, Buynak EB, Mclean AA, Hilleman MR. Long-term follow-up for immunity after monovalent or combined live measles, mumps, and rubella virus vaccine. Pediatrics 1975; **56**: 380–7.
27. Ross R, Harvey DR, Hurley R. Re-infection and congenital rubella syndrome. Practitioner 1992; **236**: 246–51.
28. Best JM, Banatvala JE, Morgan-Capner P, Miller E. Fetal infection after maternal reinfection with rubella: criteria defining reinfection. BMJ 1989; **299**: 773–5.